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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,835	10/16/2003	George Kukolj	13/083-2-C1	8470

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/686,835	KUKOLJ ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *5-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/16/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence letter*.

DETAILED ACTION

Claims 1-9 are pending.

Election/Restrictions

1. Applicant's election of Group I, claims 1-4 in species of mutation G(2042)C in the reply filed on February 23, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). However, considering the actually disclosed invention, the species election is withdrawn.

2. Claims 5-9 are withdrawn from consideration. Claims 1-4 are considered with before the examiner.

Sequence requirements

3. This application contains sequence disclosures on pages 4 and 7 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

4. Full compliance with the sequence rules is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

Priority

5. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-4 of this application. In the instant case, the current application contains a new disclosure (See pages 6, 15, 16, 22, 24-31), and the claims are directed to a content related to a host cell transfected with a self-replicating polynucleotide of HCV having mutations including G(2042)C, which are not disclosed in the provisional

application NO. 60,257,657. Therefore, the priority of current application is considered to be the filling date of parental application SN. 10,029,907, December 21, 2001.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The invention of claim 1 is directed to non-statutory subject matter. There is no recitation of isolation or synthesis in front of the claimed host cell. Therefore, the claimed compound read on naturally occurring host cell, such as a human body comprising a host cell that comprises a self-replication polynucleotide of HCV viral genome, which are considered to be non-statutory and non-patentable subject matter within the scope of 35 U.S.C. 101. See Official Gazett, 1077 O.G. April 21, 1987. It is recommended that the claim incorporate the claim language, " isolated or synthesized" to overcome this rejection.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 1 is vague in that the structural characteristic of claimed HCV self-replication polynucleotide is not defined, i.e. where does the numeric number of the first amino acid residue start. Please amend the claim with a precise sequence identification number, which enable the examiner to search and examine the claimed invention properly. Applicants can claim some additional mutation in a HCV genome; however, Office needs to know which basic non-mutated HCV genome sequence is. This affects the dependent claims 2-4.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, for reasons set forth in the objection to the specification. It appears from reading the specification that for a successful use of the claimed host cell comprising self-replicating HCV polynucleotide, the host cell line entailed in claims 1-4 is an essential element. The specification does not provide a reproducible method to make the isolated host cell comprising the particular self-replicating HCV polynucleotide or point to any direction to obtain such host cell. Hence, it would require an undue experimentation to enable the invention. Therefore, for claims that need host cell comprising self-replicating HCV replicon or obtaining such self-replicating HCV replicon, deposits of the particular host cell comprising successfully transfected HCV replicon is required.

13. For the reasons discussed above, it is apparent that the viruses specifically recited in the claims are required to practice the claimed invention. As a required element they must be known and readily available to the public or obtainable by repeatable method set forth in the specification, or otherwise readily available to the public. If not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposits of the particular HCV replicon transfected host cell line and/or deposits of the recited HCV sefl-replicon constructs See 37 CFR 1.802.

14. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

15. If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the following criteria have been met:

(a) during the pendency of this application, access to the deposits will be afforded to one determined by the commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in the public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposits will be replaced if they should become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-37 CFR 1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 112

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description in that application does not have a possession for an isolated host cell comprising a self-replicating HCV polynucleotide comprising only one mutation of G(2042)C or any other claimed mutations rather than the mutations occurred in SEQ ID NO: 2, 4, 5, 6, 7.

18. The written description requirement under Section 112, first paragraph, sets forth that the claimed subject matter must be supported by an adequate written description that is sufficient to enable anyone skilled in the art to make and use the invention. The courts have concluded that the specification must demonstrate that the inventors had possession of the claimed invention as of the filing date relied upon.

19. In the instant case, the specification only teaches isolated HCV replicon transfected Huh-7 cell clones, wherein the HCV replicon encodes SEQ ID NO: 1, 2, 4, 5 6 and 7.

20. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguished identified characteristics of the genus nucleic acid sequence. The factors to be considered include the physical and/or chemical properties, functional characteristics, structural/functional correlation, and methods of making the claimed product or any combination thereof.

21. Vas-Cath. V. Makurkar, 19USPQ2d 111, clearly states "applicant must convey with reasonable clarity to those skilled in the art, as of the filling date sough, he or she was in possession of the invention. The invention is, for purpose of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification should "clearly allow person of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Moreover, to be in the possession of any claimed invention, the applicants must show that a significance of conception and reduction to practice was reached before the application was filed. This concept is further addressed by the court in Fiers v. Sugano where it was emphasized that "[c]onception is a question of law, reviewed de novo on appeal, and if inventor is unable to envision detailed chemical structure of DNA sequence, as well as method of obtaining it, then the conception is not achieved until reduction to practice has occurred, regardless of complexity or simplicity of method of isolation.

22. Because applicants does not describe any other sequence besides SEQ ID NO: 2, 4, 5, 6, and 7, the skilled artisan cannot envision the detail chemical structure of encompassed genus nucleic acid molecule comprising at least one or more mutation listed in claim 1. An adequate written description requires more than a mere statement of what it is or what it may be or a reference to a potential method of isolating it. The compound itself is required. (See Fier v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 UQPQ2d 1016.

23. Therefore, only the host cells comprising the self-replication HCV encoded by SEQ ID NO: 2, 4, 5, 6, and 7 meet the written description provision of 35 U.S.C § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C § 112 is severable from its enablement provision (See page 1115).

Claim Rejections - 35 USC § 112

24. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

25. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for establishing a transfected host cell line comprising a particular self-replicating HCV replicon encoded by SEQ ID NO: 2, 4, 5, 7 and 6, in which the amino acid residue of Glucine at 2042 for all sequences is mutated with cystein, does not reasonably provide enablement for any other estabolished host cell comprising any HCV self-replicating polynucleotide other than the polynucleotide encoded by SEQ ID NO: 2, 4, 5, 7 or 6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

26. Nature of invention and scope of claims: The present invention is directed to several isolated transformed host cell Huh-7 clones, and each of them comprises a particular mutated HCV self-replicating polynucleotide selected from group consisting of SEQ ID NO: 2, 4, 5, 6, 7. Particular, in addition to other mutations occurred in different sequences, all of HCV

polynucleotides comprise a common mutation at amino acid residue 2042 from Glycine to Cystein (G(2042)C). The scope of claimed invention is drawn to any or all host cell comprising a self-replicating HCV replicon comprising one or more mutations as listed in claim 1.

27. State of art and unpredictability: Hepatitis C virus (HCV) is a quasisspecies of RNA virus. Currently at least six major genotypes (1-6) and a number of subtypes. Moreover, each HCV isolate exhibits different mutation. The efficiencies of the HCV replicons change greatly according to the mutation(s) randomly as evidenced by Wimmer et al. (US Patent 6, 689,559B2, see columns 1-3). However, the efficiency for a HCV 1b replicone change greatly if the HCV 5A contains some random of mutations that result in successfully isolation of several transfected Huh-7 cell clones as taught by Blight et al. (Science 2000,Vol. 290, pp. 1972-1974). However, the parental HCV replicon is much less efficient for replication and expression in the same host cell. Therefore, it is unpredictably for using other sequences for establishing a host cell that is able to replicate the virus without producing the cytotoxicity to the host cells.

28. Working example and guidance of the specification: The specification only teaches a few isolated HCV transformed Huh-7 cell clones that are able to replicate well in the transfected host cell without significantly inhibiting the host cell's viability. Applicants do not provide adequate teaching and guiding about any or all HCV replicon as claim 1 drafted that is able to transfect a host cell line without significantly inhibiting the host cell's viability.

29. Hence, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the full scope of the rejected claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Baoqun Li

Bao Qun Li M.D.
05/10/2005

Notice to Comply	Application No.	Applicant(s)	
	Examiner	Art Unit	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: see office action for detial

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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